

In the Specification:

Please amend the specification as follows:

Please delete the paragraph on page 13, lines 28-29, and replace it with the following paragraph:

FIGURE 5 is a schematic representation of the sequence of human alpha-3 chain globular domain peptides disclosed herein (SEQ ID NO:31).

Please delete the paragraph on page 13, lines 30-31, and replace it with the following paragraph:

FIGURE 6 is a schematic representation of the sequence of murine alpha-4 chain globular domain peptides disclosed herein (SEQ ID NO: 32).

Please delete the paragraph on page 14, lines 1-2, and replace it with the following paragraph:

FIGURE 7 is a schematic representation of the sequence of murine alpha-5 chain globular domain peptides disclosed herein (SEQ ID NO: 33).

Please delete the paragraph on page 14, lines 3-4, and replace it with the following paragraph:

FIGURE 8 is a table which includes laminin globular domain-derived peptides (SEQ ID NOS 1, 20-21, 2, 22, 3, 23 4-6, 24, 7, 25, 8-10, 26, 11-12, 27-28, 13, 29, 14-19, and 30, respectively in order of appearance) which can disrupt/ disassemble pre-formed Alzheimer's A $\beta$  1-40 fibrils.

Please delete the paragraph on page 14, lines 10-11, and replace it with the following paragraph:

FIGURES 12a-f are laminin-derived peptide sequences for 12-13 mer peptides DP1-18 and LP19-25, and 7 mer peptides DP 26-49 (SEQ ID NOS 1, 3, 8, 11, 15, 18, 4-5, 7, 10, 16, 19, 34-39, 1, 3, 8, 40, 15, 18, and 41-65, respectively in order of appearance).

Please delete the paragraph on page 18, lines 18-22, and replace it with the following paragraph:

As used here in "A $\beta$  amyloidoses" refers to amyloid diseases which involve the formation, deposition, accumulation and/or persistence of A $\beta$  (i.e. beta-amyloid protein), including but not limited to A $\beta$  containing 39-43 amino acids in length, but more preferably, A $\beta$  1-40 (~~SEQ ID NO:36~~), or A $\beta$  1-42 (~~SEQ ID NO:37~~), and mixtures or fragments thereof.

Please delete the paragraph on page 22, line 32, to page 23, line 28, and replace it with the following paragraph:

These selected laminin globular domain-derived peptides were then tested for their effectiveness to also disrupt/disassemble pre-formed A $\beta$  1-42 fibrils (Figure 9). In this latter study, selected laminin globular domain-derived peptides were incubated with pre-formed A $\beta$  1-42 fibrils at an A $\beta$ :peptide molar ratio of 1:10. Direct comparisons were made to iA $\beta$ 5, a 5 amino-acid (LPFFD; SEQ ID NO: 41) A $\beta$  inhibitor previously identified as a potent inhibitor of A $\beta$  fibrillogenesis (Soto et al, Nature Med. 4:822-826, 1998). The results demonstrate that six laminin globular domain-derived peptides were significantly more effective than iA $\beta$ 5 in causing a disruption/disassembly of preformed A $\beta$  1-42 fibrils (Figure 9). These laminin-derived peptides included peptides from the laminin alpha-1 chain [(i.e. AG73 - SEQ ID NO:1; A13 -SEQ ID NO 3), the laminin alpha-3 chain (i.e. HA3G76 - SEQ ID NO:8), the laminin alpha-4 chain (i.e.

A4G82 - SEQ ID NO: 11) and the laminin alpha-5 chain (i.e. A5G81- SEQ ID NO:15; A5G101 - SEQ ID NO: 18). It should be noted that two of these A $\beta$  inhibiting peptides were derived from the globular domain of the laminin alpha-1 chain, and the more effective of these two peptides (i.e. AG73 -SEQ ID NO:1) was precisely located within the 4th globular domain of the laminin-1 chain, and found to bind very tightly to A $\beta$  (Fig. 8). In our studies (described above), the AG73 (SEQ ID NO:1) peptide disrupted A $\beta$  1-42 fibrils by 81 % when used at an A $\beta$ :peptide molar ratio of 1:10. In comparison, this peptide was 31 % more effective than the previously described iA $\beta$ 5 peptide (Soto et al, Nature Med. 4:822-826 1998), which in our studies only dissociated pre-formed A $\beta$  1-42 fibrils by 50%. At an A $\beta$ :peptide molar ratio of 1:2, the AG73 peptide (SEQ ID NO:1) was also found to disrupt/disassemble pre-formed A $\beta$  1-42 fibrils by 72 %, whereas the iA $\beta$ 5 peptide only caused a 27% disruption/disassembly (Figure 9). The other laminin fragment reported in the literature (Monji et al, Neurosc. Lett. 251:65-68, 1998) required an A $\beta$ :peptide molar ratio of 1:10 to obtain a 50% inhibition of A $\beta$  fibril formation, whereas our newly identified AG73 peptide (SEQ ID NO:1) only required an A $\beta$ :peptide molar ratio of 1:1 to achieve the same level of inhibition. Assuming that the 12-amino acid peptide, AG73 (SEQ ID NO:1), represents a single-site of A $\beta$  binding, we can be confident that we are close to theoretically optimum inhibition. During this screening process, we also identified 5 other peptides in the alpha 3, 4, and 5 chains that were most effective in disrupting/ causing a disassembly of pre-formed A $\beta$  fibrils (see Figure 8).

Please delete the paragraph on page 32, line 21, to page 33, line 4, and replace it with the following paragraph:

We have now synthesized the D-form of the 6 parent 12-13 amino acid peptides discussed above as Sequence Group B (all L-forms) as showing superior A $\beta$  amyloid inhibitory activity. Since we earlier tested the L-form of each of the 6 laminin derived peptides, we chose to

synthesize the D-amino acid form of the same 6 laminin derived peptides. Those D-form amino acids synthesized are: DP1) AG73 (RKRLQVQLSIRT) (SEQ ID NO: 1), DP2) A13 (RQVFQVAYIIKA) (SEQ ID NO: 3), DP3) HA3G76 (YLSKGRLVFALG) (SEQ ID NO: 8), DP4) A4G82 (TLFLAHGRLVFM) (SEQ ID NO: 11), DP5) A5G81 (AGQWHRVSVRWG) (SEQ ID NO: 15), and DP6) A5G101 (DGRWHRVAVIGM) (SEQ ID NO: 18). The D amino acid form of these peptides is believed to offer some therapeutic advantage over L-form peptides, since the D amino acid peptides are known to be more resistant to *in vivo* protease degradation. In addition, the reverse sequences (DP13-18) of all 6 D-form peptides described above were also synthesized to determine if reversing the sequence alters potential A $\beta$  amyloid inhibitory activity. Lastly, a group of another 6 D amino acid 12-13 mer peptides (DP7-12) were also synthesized, and these represents 6 additional laminin derived peptides (also already tested in L amino acid form) that were only somewhat less effective than the first 6 peptides described above, still maintaining >25% A $\beta$  fibril disrupting ability.

Please delete the paragraph on page 33, lines 8-11, and replace it with the following paragraph:

For example, representative DP1 D-AG73 peptide truncations (the resulting 7 L- or D-amino acid peptides synthesized and tested for amyloid inhibitory activity) are RKRLQVQ(Y) (SEQ ID NO: 66), KRLQVQL(Y) (SEQ ID NO: 67), RLQVQLS(Y) (SEQ ID NO: 68), LQVQLSI(Y) (SEQ ID NO: 69), QVQLSIR(Y) (SEQ ID NO: 70) and, VQLSIRT(Y) (SEQ ID NO: 71).

Please delete the paragraph on page 33, lines 12-14, and replace it with the following paragraph:

For example, for DP2 D-A13 peptide truncation, a resulting (7 L- or D-amino acid) peptides synthesized and tested for amyloid inhibitory activity is RQVFQϣVA (SEQ ID NO: 72), QVFQϣVAY (SEQ ID NO: 73), VFQϣVAYI (SEQ ID NO: 74), FQϣVAYII (SEQ ID NO: 75), QϣVAYIII (SEQ ID NO: 76), ϣVAYIIK (SEQ ID NO: 77), and AYIIKA (SEQ ID NO: 78).

Please delete the paragraph on page 33, lines 15-17, and replace it with the following paragraph:

For example, for DP3 D-HA3G76 peptide truncation, a resulting (7 L- or D-amino acid) peptides synthesized and tested for amyloid inhibitory activity is YLSKGRL(Y) (SEQ ID NO: 79), LSKGRLV(Y) (SEQ ID NO: 80), SKGRLVF(Y) (SEQ ID NO: 81), KGRLVFA(Y) (SEQ ID NO: 82), GRLVFAL(Y) (SEQ ID NO: 83), and RLVFALG(Y) (SEQ ID NO: 84).

Please delete the paragraph on page 33, lines 18-21, and replace it with the following paragraph:

For example, for DP4 D-A4G82 peptide truncation, a resulting (7 L- or D-amino acid) peptides synthesized and tested for amyloid inhibitory activity is DP38 TLFLAHG(Y) (SEQ ID NO: 85), DP39 LFLAHGR(Y) (SEQ ID NO: 86), DP40 FLAHGRL(Y) (SEQ ID NO: 87), DP41 LAHGRLV(Y) (SEQ ID NO: 88), DP42 AHGRLVF(Y) (SEQ ID NO: 89), and DP43 HGRLVFM(Y) (SEQ ID NO: 90).

Please delete the paragraph on page 33, lines 22-25, and replace it with the following paragraph:

For example, for DP5 D-A5G81 peptide truncation, a resulting (7 L- or D-amino acid) peptides synthesized and tested for amyloid inhibitory activity is DP 26 AGQWHRV(Y) (SEQ ID

NO: 91), DP27 GQWHRVS(Y) (SEQ ID NO: 92), DP28 QWHRVSV(Y) (SEQ ID NO: 93), DP29 WHRVSVR(Y) (SEQ ID NO: 94), DP30 HRVSVRW(Y) (SEQ ID NO: 95), and DP31 RVSVRWG(Y) (SEQ ID NO: 96).

Please delete the paragraph on page 33, lines 26-29, and replace it with the following paragraph:

For example, for DP6 D-A5G101peptide truncation, a resulting (7 L- or D-amino acid) peptides synthesized and tested for amyloid inhibitory is DP 32 DGRWHRV(Y) (SEQ ID NO: 97), DP33 GRWHRVA(Y) (SEQ ID NO: 98), DP34 RWHRVAV(Y) (SEQ ID NO: 99), DP35 WHRVAVI(Y) (SEQ ID NO: 100), DP36 HRVAVIM(Y) (SEQ ID NO: 101), and DP37 RVAVIMG(Y) (SEQ ID NO: 102).

Please delete the paragraph on page 33, line 30, to page 34, line 2, and replace it with the following paragraph:

In addition, for DP15 D-R-HA3G76 peptide truncation, a resulting (7 L- or D-amino acid) peptides synthesized and tested for amyloid inhibitory activity is DP44 GLAFVLR(Y) (SEQ ID NO: 103), DP45 LAFVLRG(Y) (SEQ ID NO: 104), DP46 AFVLRGK(Y) (SEQ ID NO: 105), DP47 FVLRGKS(Y) (SEQ ID NO: 106), DP48 VLRGKSL(Y) (SEQ ID NO: 107), and DP49 LRGKSLY(Y) (SEQ ID NO: 108).

Respectfully submitted,



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